patients, donor hematopoiesis is accounted for by one unit, although the mechanisms of unit dominance are not established. Cord blood NK cells are predominantly of a mature phenotype, with cytotoxic activity following IL-2 stimulation comparable to peripheral blood NK cells, but with higher proliferation capacity. We, therefore, hypothesized that NK cells may determine unit dominance following DCBT. We examined KIR haplotypes of each unit, and the unit-unit and unit-recipient KIR-HLA interactions in 83 DCBT recipients transplanted at MSKCC between October 2005 and July 2010 for hematological malignancies. Median age of patients was 35.6 years (0.9-64.6). Patients received myeloablative (n = 65) or non-myeloablative (n = 18) conditioning, and immunosuppression with a calcineurin inhibitor and mycophenolate mofetil. Chi-square test was used to examine the frequency distributions differences of specific KIR haplotypes and individual activating KIR between the predominating and the non-engrafting units. It was also used to test equal frequency distributions of inhibitory KIR-mediated missing ligand or missing self. Group B-haplotypes (34.9% vs. 41.4%, p = 0.2) were not associated with a higher likelihood of unit dominance. Similarly, none of the individual activating KIR showed any association with unit dominance. The majority of unit pairs either had no KIR-HLA combinations predictive of NK alloreactivity (n = 20), or had NK alloreactivity predicted to occur in a bidirectional manner (n = 35). Results from unit-unit interaction analyses showed that units missing KIR ligand (16/29 vs 13/29, p = 0.71), or lacking class I determinants present in the second unit (12/18 vs 6/18, p = 0.23), did not show a lower rate of engraftment. For unit-recipient interactions, cord blood units did not have a higher likelihood of engraftment even if the patient was missing ligand for the unit inhibitory KIR (2/7 vs. 5/7, p = 0.45), or lacked class I determinants present in the unit (7/16 vs. 9/16 p = 0.80). Results from recipient-unit interaction analyses revealed that units missing KIR ligand (12/25 vs. 13/25, p = 1.00) or lacking class I determinants present in the recipient (9/19 vs. 10/19, p = 1.00) did not show a lower rate of engraftment. In this cohort of DUCBT, we could not demonstrate a role for KIR-HLA genotypes or KIR haplotypes in predicting cord unit predominance.

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4-LOG EX-VIVO T-LYMPHOCYTE DEPLETED MYELOABLATIVE HLA-MATCHED SIBLING TRANSPLANTS; A PLATFORM FOR ADOPTIVE IMMUNOTHERAPY INFLUENCED BY CONDITIONING INTENSITY

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Allogeneic hematopoietic stem cell transplantation(HSCT) must serve as a platform for adoptive cellular immunotherapy to fully exploit graft versus leukemia effects. We have developed a 4-log ex-vivo T lymphocyte depleted HSCT with minimal graft versus host disease (GvHD) prophylaxis followed by elective donor lymphocyte infusion at day 90. A lymphodepleted environment without immunosuppression would favor homeostatic expansion of adoptively infused cells in future protocols. 39 patients with hematologic malignancies underwent allogeneic HSCT with a graft from their HLA-identical siblings. The median age was 41 years (range 16-68), 17/39 were males. Transplant indications were AML(18), ALL(8), acute biphenotypic leukemia(1), MDS(7), NHL/CLL(3), CMMoL(1) and CML(1). 50% were standard risk and 50% were at high risk for relapse. Subjects received myeloablative conditioning with cyclophosphamide (60 mg/kg/dose x 2), fludarabine (25 mg/m2/dose x 5) and total body irradiation (12 Gy in 8 fractions, lungs shielded to 6Gy). Ten subjects, who were 55 years of age or older, received 4 Gy divided in 8 fractions without lung shielding. G-CSF mobilized peripheral blood grafts from the donor were CD34+ selected (Miltenyi CliniMacs), with infusion of a target CD34+ dose of 6x10e6/kg and a fixed CD3+ dose of 5x10e4/kg. Low-dose cyclosporine (100-200ng/mL) till day 21 was the only GVHD prophylaxis. Delayed lymphocyte add back (5x10e6 CD3+/kg) was given at day 90 if patients had no significant GVHD. CD3+ and myeloid chimerism analyses were performed with early lymphocyte add-back in cases with falling chimerism. Day 200 overall survival (the primary study endpoint) was 84%. One patient, who was postpartum, failed to engraft and required a second transplant. 37/39 subjects achieved complete (> 95%) donor myeloid chimerism by day14. The median times to complete donor CD3+ chimerism were day30 for 12 Gy subjects and > 6 months for 4 Gy subjects (Mann Whitney test, p = 0.004). The incidence of acute GVHD grade II, III and IV were 23%, 2.9% and 0%, respectively. The incidence of chronic GVHD was 34%. At a median follow up of 3.7 years, Kaplan-Meier estimates of relapse, nonrelapse mortality and overall survival were 32%, 31% and 46% respectively without any significant difference based on conditioning intensity. In conclusion, conditioning intensity influences the rapidity of complete donor CD3+ chimerism in transplants utilizing this platform for adoptive cellular immunotherapy.

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BONE MARROW OR PERIPHERAL BLOOD STEM CELL TRANSPLANTATION FROM UNRELATED DONORS IN ADULT PATIENTS WITH ACUTE MYELOID LEUKEMIA

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In leukemia patients, peripheral blood stem cells (PBSC) have replaced bone marrow (BM) as stem cell source. No study has shown any benefit using PBSC versus BM in matched unrelated donor (MUD) transplantation. We therefore compared PBSC and BM in MUD recipients with acute myeloid leukemia (AML).

Between 1997 and 2008, 760 patients received BM and 1,502 PBSC from a MUD. The PBSC group were older age (p < 0.01), had more advanced disease (p < 0.0001), received less total body irradiation (p < 0.0001), and more antithymocyte globulin (p = 0.01). Recovery of neutrophils and platelets was faster with PBSC (p < 0.0001). Acute GVHD was similar, but chronic GVHD was increased in the PBSC group (HR 1.29, p = 0.02). Non-relapse mortality (NRM), relapse and leukemia-free survival (LFS) did not differ between the two groups, in AML patients in remission. However, in patients with advanced AML, NRM was decreased (HR 0.61, p = 0.02) and LFS was improved (HR 1.49, p = 0.002) using PBSC. At 3 years, LFS for all patients, regardless of remission status, was 41±1% for both groups.

PBSC compared to BM in MUD transplants in AML resulted in: faster neutrophil and platelet recovery, not statistically different acute GVHD, increased chronic GVHD and same rates of LFS in remission patients. In advanced AML, the PBSC group had decreased NRM and improved LFS.

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THE DOUBLE BENEFIT OF EX-VIVO GENERATED ANTI 3RD PARTY CD8 T CELLS WITH CENTRAL MEMORY PHENOTYPE: ENHANCED BM ENGRAFTMENT COUPLED WITH MARKED GVL IN THE ABSENCE OF GVHD

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Achieving engraftment of T cell depleted BMT under reduced intensity conditioning (RIC) remains a major challenge. Recently, we demonstrated that anti 3rd-party CD8 T cells with ex-vivo induced central memory phenotype (Tcm) can enhance BM engraftment